

Request. — Jan Deluca

Access DB# 138837

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabine Woz Examiner #: 74141 Date: 8/23/04  
Art Unit: 1616 Phone Number: 301 20622 Serial Number: 10/763, 710  
Mail Box and Bldg/Room Location: 4C70 Rm 4A45 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: (205) 1 - alpha hydroxy 2 alpha methyl 19-nor

Inventors (please provide full names): Deluca et al

Earliest Priority Filing Date: 4/22/2002

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

23-28

Please search for a method of treating a skin condition as in cl 23-28.

Please search for all the stereoisomers and a broader search at 2-position

Related cases

Thank you

10/763, 029  
10/763, 023  
10/762, 618  
10/762, 906  
10/127, 180

### STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: <u>Jan</u>	NA Sequence (#) <u>STN</u>	<u>✓</u>
Searcher Phone #: <u>22504</u>	AA Sequence (#) <u>Dialog</u>	
Searcher Location: <u>8/25</u>	Structure (#) <u>✓</u>	Questel/Orbit
Date Searcher Picked Up: <u>8/25</u>	Bibliographic	Dr. Link
Date Completed: <u>8/25</u>	Litigation	Lexis/Nexis
Searcher Prep & Review Time: <u>15</u>	Fulltext	Sequence Systems
Clerical Prep Time: <u>15</u>	Patent Family	WWW/Internet
Online Time: <u>120</u>	Other	Other (specify)

=> fil reg

FILE 'REGISTRY' ENTERED AT 10:09:50 ON 25 AUG 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

DICTIONARY FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d l13 ide can tot

L13 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 618104-21-5 REGISTRY

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C27 H44 O2

SR CA

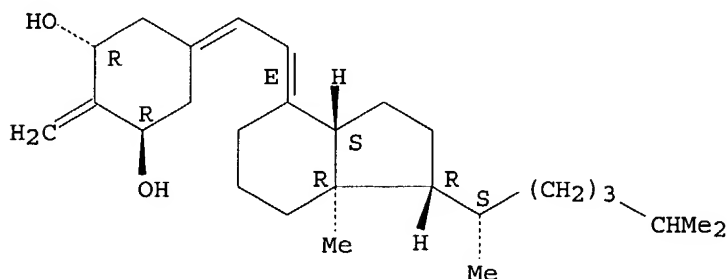
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

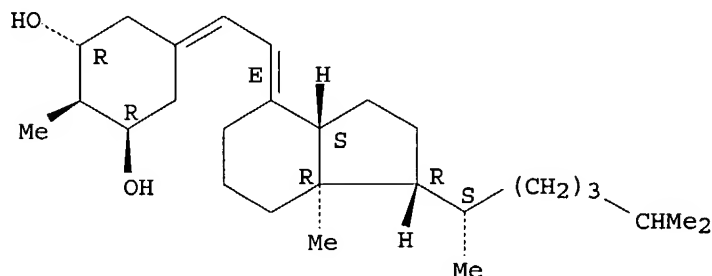
REFERENCE 1: 139:345953

L13 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 618104-20-4 REGISTRY

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C27 H46 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA CAPLUS document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:345953

=> fil hcaplus  
FILE 'HCAPLUS' ENTERED AT 10:09:58 ON 25 AUG 2004  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1907 - 25 Aug 2004 VOL 141 ISS 9  
FILE LAST UPDATED: 24 Aug 2004 (20040824/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr l19

L19 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:855808 HCAPLUS

DN 139:345953  
 ED Entered STN: 31 Oct 2003  
 TI (20S)-1 $\alpha$ -Hydroxy-2 $\alpha$ -methyl--19-nor-vitamin D3 and  
 (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl--19-nor-vitamin D3, and  
 pharmaceutical uses  
 IN Deluca, Hector F.; Sicinski, Rafal R.; Grzywacz, Pawel K.  
 PA Wisconsin Alumni Research Foundation, USA  
 SO PCT Int. Appl., 44 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-593  
 ICS A61P017-06; A61P019-10; A61P035-00; A61P037-06  
 CC 1-12 (Pharmacology)  
 Section cross-reference(s): 32, 63

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003088977	A1	20031030	WO 2003-US8423	20030320
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003203882	A1	20031030	US 2002-127180	20020422
	US 2004152675	A1	20040805	US 2004-762618	20040122
	US 2004152676	A1	20040805	US 2004-762710	20040122
	US 2004152677	A1	20040805	US 2004-762906	20040122
	US 2004152678	A1	20040805	US 2004-762911	20040122
	US 2004152679	A1	20040805	US 2004-763023	20040122
	US 2004152680	A1	20040805	US 2004-763029	20040122
PRAI	US 2002-127180	A	20020422		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003088977	ICM	A61K031-593
	ICS	A61P017-06; A61P019-10; A61P035-00; A61P037-06

AB The invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D3 and pharmaceutical uses therefor. These compds. exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases, e.g. psoriasis, as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compds. also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases, e.g. osteoporosis. Compound preparation is described.

ST norvitamin D3 deriv prepn therapeutic; antitumor skin condition therapy norvitamin D3 deriv; immune disease osteoporosis norvitamin D3 deriv; metabolic bone disease norvitamin D3 deriv

IT Animal cell line  
 (HL-60; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Bone  
 (bone mass increase; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Biological transport  
 (calcium; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Intestine, neoplasm

(colon; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drugs  
(gastrointestinal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Transplant and Transplantation  
(host-vs.-graft reaction; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Hydration, physiological  
(inadequate dermal hydration; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Cell differentiation  
(inducers; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Intestine, disease  
(inflammatory; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Sebum  
(insufficient secretion; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Osteoporosis  
(low bone turnover osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Anti-inflammatory agents  
Antiasthmatics  
Antidiabetic agents  
Antirheumatic agents  
Antitumor agents  
Asthma  
Autoimmune disease  
Cell differentiation  
Diabetes mellitus  
Human  
Inflammation  
Leukemia  
Lupus erythematosus  
Mammary gland, neoplasm  
Monocyte  
Multiple sclerosis  
Osteomalacia  
Prostate gland, neoplasm  
Psoriasis  
Rheumatoid arthritis  
Transplant rejection  
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT Vitamin D receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems  
(oral; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Bone, disease  
(osteopenia; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems  
(parenterals; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Osteoporosis  
(postmenopausal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Myelocyte  
(promyelocyte; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Aging, animal  
(senile osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Steroids, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(steroid-induced osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems  
(topical; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems

(transdermal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Skin  
(wrinkles and other conditions; nor-vitamin D3 derivs. and pharmaceutical uses)

IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT 618104-20-4P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT 50-14-6, Vitamin D2 98-59-9, p-Toluenesulfonyl chloride 98-88-4, Benzoyl chloride 4237-74-5 213250-64-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT 64190-52-9P 66774-70-7P 66774-71-8P 115527-12-3P 145354-28-5P 235108-01-7P 235108-02-8P 618104-21-5P 618104-22-6P 618879-43-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

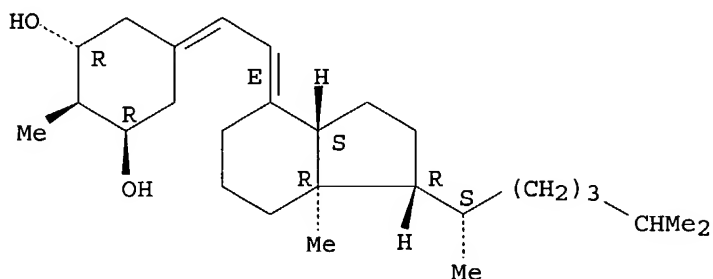
(1) Bouillon, R; ENDOCRINE REVIEWS 1995, V16(2), P200 HCAPLUS  
(2) Castedo, L; TETRAHEDRON LETTERS 1986, V27(13), P1523 HCAPLUS  
(3) Deluca, H; US 6306844 B1 2001 HCAPLUS  
(4) Sicinski, JOURNAL OF MEDICINAL CHEMISTRY 1998, V41, P4662 HCAPLUS

IT 618104-20-4P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



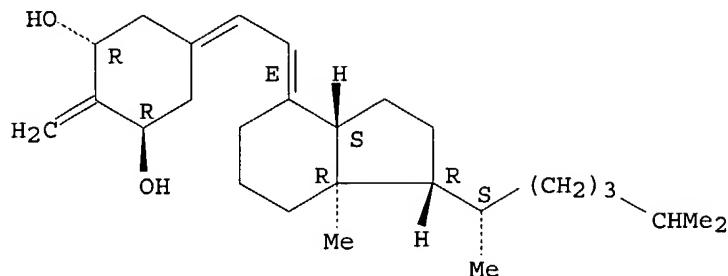
IT 618104-21-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



=> fil uspatall

FILE 'USPATFULL' ENTERED AT 10:10:13 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:10:13 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr tot l20

L20 ANSWER 1 OF 7 USPATFULL on STN

AN 2004:197374 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152680 A1 20040805

AI US 2004-763029 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE

1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 981

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D<sub>3</sub> and (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D<sub>3</sub> and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

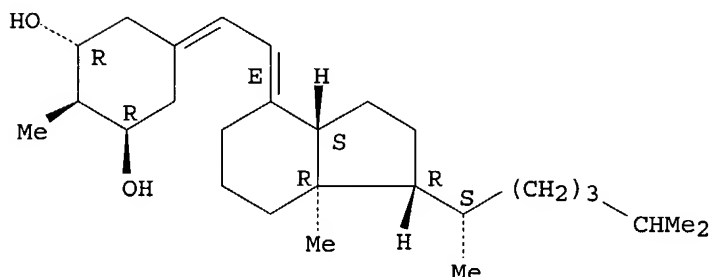
IT 618104-20-4P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



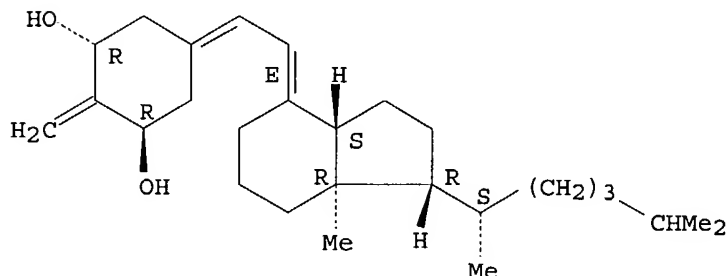
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L20 ANSWER 2 OF 7 USPATFULL on STN

AN 2004:197373 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152679 A1 20040805

AI US 2004-763023 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1α-hydroxy-2α-methyl-19-nor-



vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

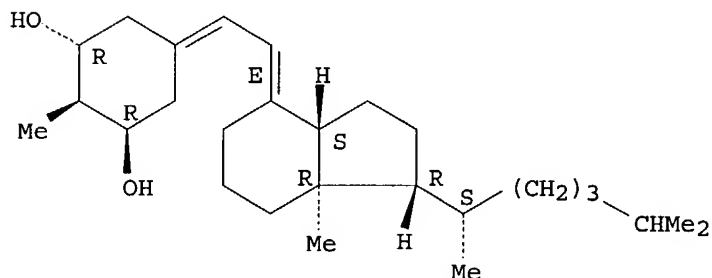
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 618104-21-5P

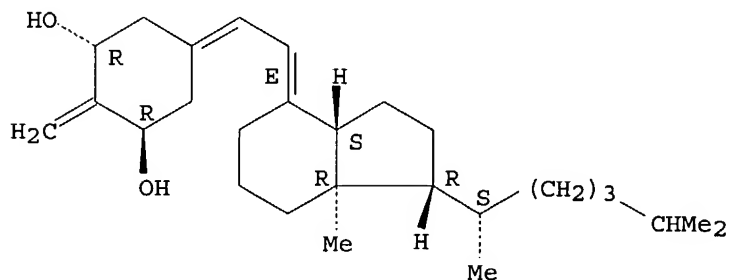
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 3 OF 7 USPATFULL on STN

AN 2004:197372 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES  
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)  
 PI US 2004152678 A1 20040805  
 AI US 2004-762911 A1 20040122 (10)  
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

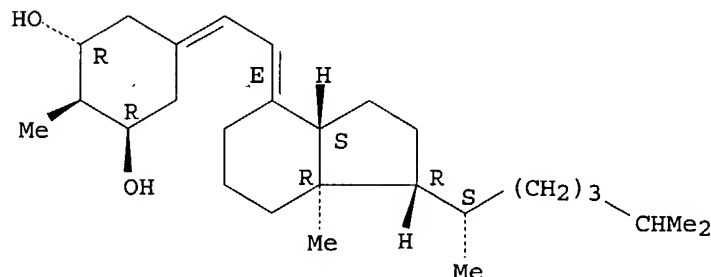
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPTFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 618104-21-5P

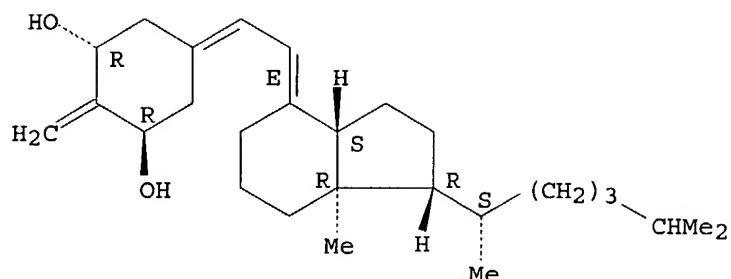
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPTFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 4 OF 7 USPTFULL on STN  
 AN 2004:197371 USPTFULL  
 TI (20S)-1α-hydroxy-2α-methyl and 2β-methyl-19-nor-vitamin D3 and their uses  
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Sicinski, Rafal R., Warsaw, POLAND  
 Grzywacz, Pawel K., Madison, WI, UNITED STATES  
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)  
 PI US 2004152677 A1 20040805  
 AI US 2004-762906 A1 20040122 (10)  
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 980

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1α-hydroxy-2α-methyl-19-nor-vitamin D.sub.3 and (20S)-1α-hydroxy-2β-methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

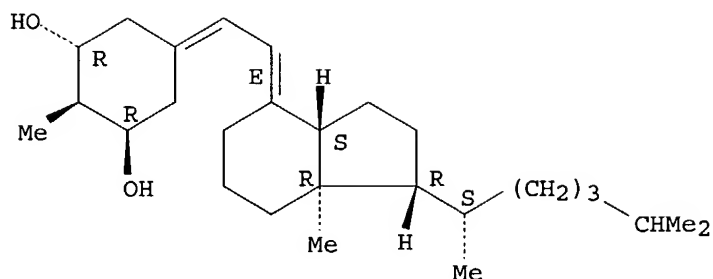
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPTFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 618104-21-5P

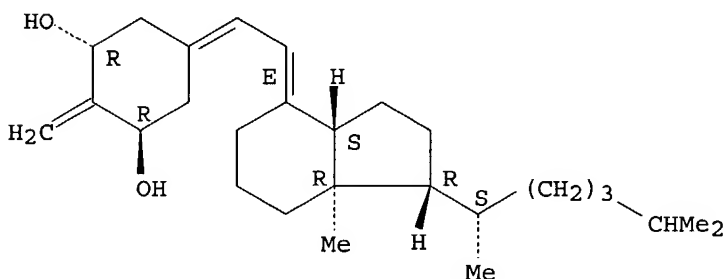
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 5 OF 7 USPATFULL on STN

AN 2004:197370 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152676 A1 20040805

AI US 2004-762710 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 978

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin,

dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

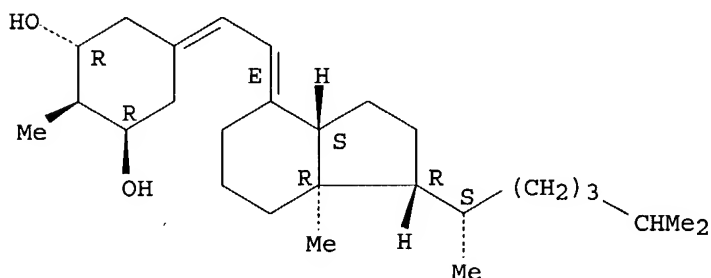
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 618104-21-5P

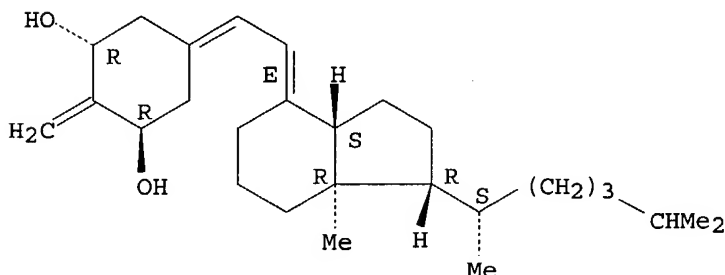
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 6 OF 7 USPATFULL on STN

AN 2004:197369 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)

PI US 2004152675 A1 20040805

AI US 2004-762618 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

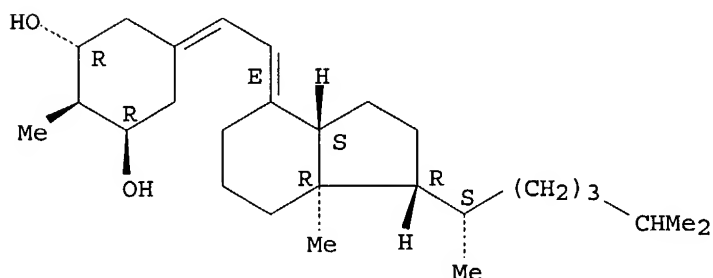
IT 618104-20-4P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



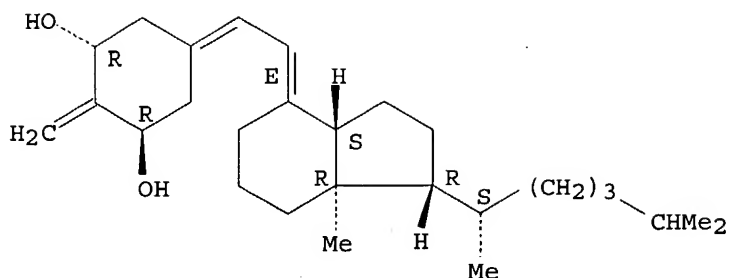
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L20 ANSWER 7 OF 7 USPATFULL on STN

AN 2003:289123 USPATFULL

TI (20S) 1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PI US 2003203882 A1 20031030

AI US 2002-127180 A1 20020422 (10)

DT Utility

FS APPLICATION

LREP KINNEY & LANGE, P.A., THE KINNEY & LANGE BUILDING, 312 SOUTH THIRD STREET, MINNEAPOLIS, MN, 55415-1002

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

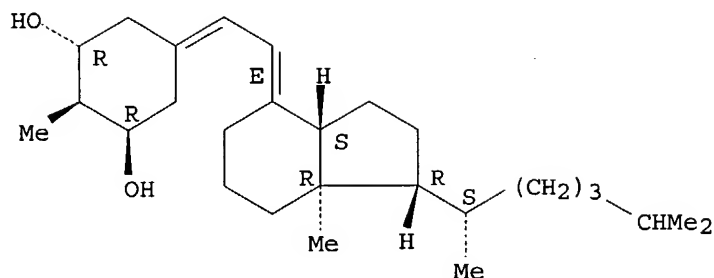
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



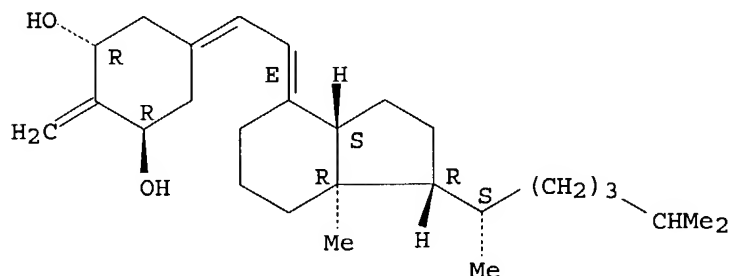
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



=&gt; =&gt; fil reg

FILE 'REGISTRY' ENTERED AT 10:15:55 ON 25 AUG 2004

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provided by InfoChem.

STRUCTURE FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

DICTIONARY FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

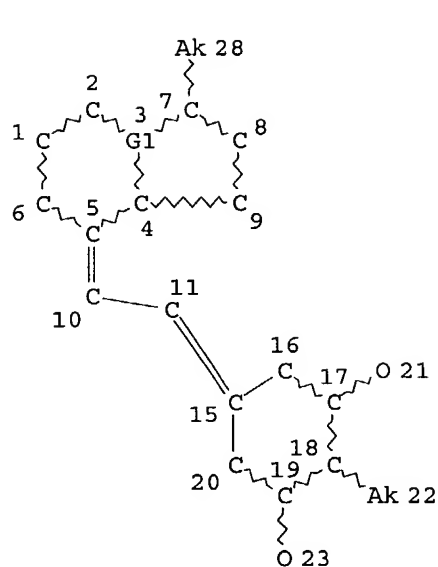
Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=&gt; d sta que 125

L23

STR





27  
Ak  
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C  
@25

VAR G1=C/25

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 21

CONNECT IS M1 RC AT 23

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 7356 ITERATIONS

SEARCH TIME: 00.00.01

8 ANSWERS

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SEL RN

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L2 17 S E1-E17

L3 1 S L2 AND C27H46O2  
E C27H46O2/MF

L4 19 S E3 AND C5-C6/ES AND C6/ES AND 3/NR NOT 46.150.18/RID  
SEL RN L3

L5 0 S E1/CRN

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L6 0 S L3

FILE 'HCAPLUS' ENTERED AT 10:06:07 ON 25 AUG 2004

L7 1 S L3

L8 FILE 'USPATFULL, USPAT2' ENTERED AT 10:06:11 ON 25 AUG 2004  
7 S L3

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FILE 'HCAPLUS' ENTERED AT 10:06:31 ON 25 AUG 2004

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FILE 'REGISTRY' ENTERED AT 10:07:13 ON 25 AUG 2004  
L9 8 S L2 AND C5-C6/ES AND C6/ES NOT L3  
L10 3 S L9 NOT 46.150.18/RID  
L11 2 S L10 NOT SI/ELS  
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L13 2 S L3,L12  
E C27H44O2/MF  
L14 117 S E3 AND C5-C6/ES AND C6/ES AND 3/NR NOT 46.150.18/RID  
L15 1 S L14 AND 1 3 CYCLOHEXANEDIOL  
L16 2 S L14 AND METHYLENE  
SEL RN L12  
L17 0 S E1/CRN

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L18 0 S L13

FILE 'HCAPLUS' ENTERED AT 10:09:37 ON 25 AUG 2004  
L19 1 S L13

FILE 'USPATFULL, USPAT2' ENTERED AT 10:09:42 ON 25 AUG 2004  
L20 7 S L13

FILE 'REGISTRY' ENTERED AT 10:09:50 ON 25 AUG 2004

FILE 'HCAPLUS' ENTERED AT 10:09:58 ON 25 AUG 2004

FILE 'USPATFULL, USPAT2' ENTERED AT 10:10:13 ON 25 AUG 2004

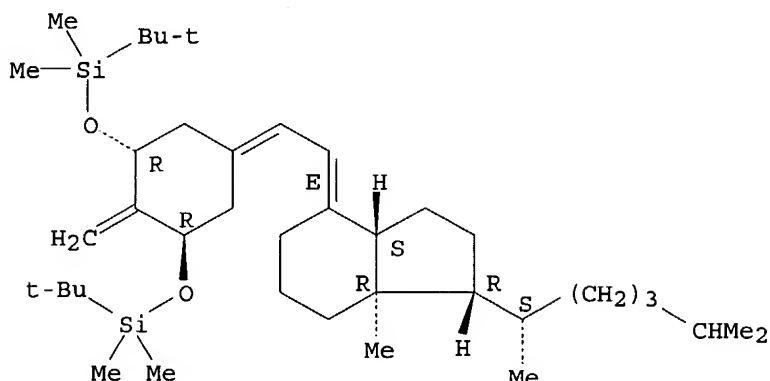
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L22 0 S L21 CSS  
L23 STR L21  
L24 1 S L23 CSS  
L25 8 S L23 CSS FUL  
SAV L25 QAZI762/A  
L26 6 S L25 NOT L13

FILE 'REGISTRY' ENTERED AT 10:15:55 ON 25 AUG 2004

=> d ide can tot l26

L26 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 618104-22-6 REGISTRY  
CN Silane, [(1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-  
5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl- (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C39 H72 O2 Si2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA Caplus document type: Patent  
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.  
Double bond geometry as shown.



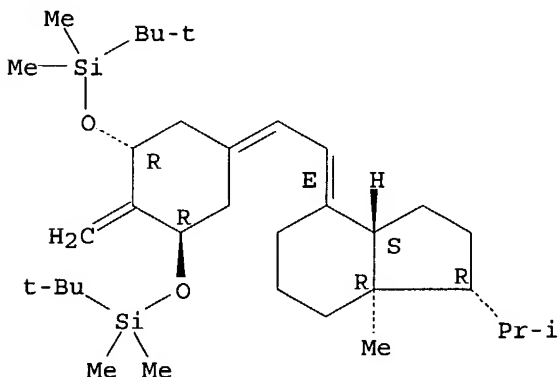
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:345953

L26 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 610304-71-7 REGISTRY  
CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C34 H62 O2 Si2  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL  
DT.CA Caplus document type: Patent  
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

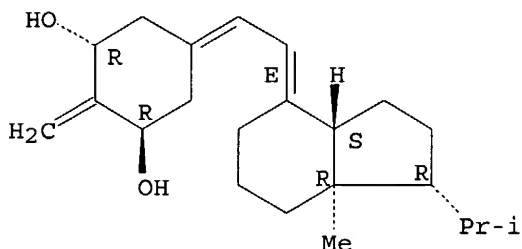
1 REFERENCES IN FILE CA (1907 TO DATE)

## 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:307926

L26 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 524067-22-9 REGISTRY  
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H34 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL  
 DT.CA Caplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation)  
 RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)  
 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:82860

REFERENCE 2: 139:317525

REFERENCE 3: 139:307926

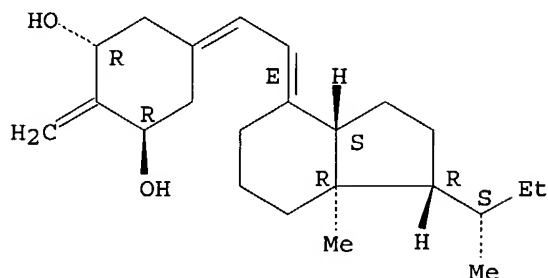
REFERENCE 4: 138:363223

L26 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 524067-21-8 REGISTRY  
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

## OTHER NAMES:

CN (20S)-1 $\alpha$ -Hydroxy-2-methylene-19-norbishomopregnacalciferol  
 CN Becocalcidiol  
 CN QRX 101  
 FS STEREOSEARCH  
 MF C23 H36 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, PROUSDDR, TOXCENTER, USPAT2, USPATFULL  
 DT.CA Caplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:82860

REFERENCE 2: 140:386155

REFERENCE 3: 139:53211

REFERENCE 4: 138:363223

L26 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN

RN 524067-20-7 REGISTRY

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C21 H32 O2

SR CA

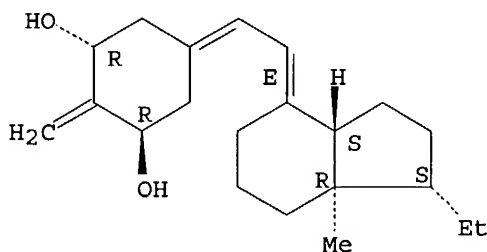
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:82860

REFERENCE 2: 138:363223

L26 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN

RN 403647-27-8 REGISTRY

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethyldene]-, (1R,3R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C22 H34 O2

SR CA

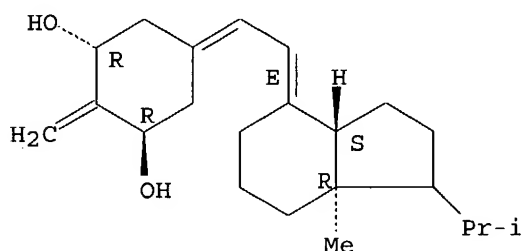
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:335278

REFERENCE 2: 136:226818

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ACT QAZI762/A

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L2 8 SEA FILE=REGISTRY CSS FUL L1

L3 6 S L2 NOT (618104-21-5 OR 618104-20-4)

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L4 0 S L3

FILE 'HCAPLUS' ENTERED AT 10:21:18 ON 25 AUG 2004

L5 9 S L3

L6 6 S L5 AND (PD<=20020422 OR PRD<=20020422 OR AD<=20020422)

L7 9 S L5 AND (DELUCA ? OR DE LUCA ? OR SICINSKI ? OR GRZYWACZ ?)/AU

L8 9 S L5-L7

FILE 'USPATFULL, USPAT2' ENTERED AT 10:22:34 ON 25 AUG 2004  
L9 18 S L3

L10 18 S L9 AND (DELUCA ? OR DE LUCA ? OR SICINSKI ? OR GRZYWACZ ?)/A

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 10:23:03 ON 25 AUG 2004

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FILE COVERS 1907 - 25 Aug 2004 VOL 141 ISS 9

FILE LAST UPDATED: 24 Aug 2004 (20040824/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 18 all hitstr tot

L8 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:413892 HCAPLUS

DN 141:82860

ED Entered STN: 21 May 2004

TI Biologically active noncalcemic analogs of 1 $\alpha$ ,25-dihydroxyvitamin D with an abbreviated side chain containing no hydroxyl

AU Plum, Lori A.; Prahl, Jean M.; Ma, Xiaohong; Sicinski, Rafal R.; Gowlugari, Sumithra; Clagett-Dame, Margaret; DeLuca, Hector F.

CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2004), 101(18), 6900-6904  
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 2-10 (Mammalian Hormones)

AB Since the discovery of the active metabolite of vitamin D, i.e., 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>, there has been a continuous effort to synthesize analogs able to carry out many of the functions of the native hormone without raising serum calcium concentration. The present report provides

a series of previously undescribed analogs wherein this goal is realized. The authors have prepared 2-methylene-19-nor-1 $\alpha$ -hydroxyvitamin D analogs of 1,25-(OH)<sub>2</sub>D<sub>3</sub> that possess only two to four carbons of the side chain without a hydroxyl thereon. Compared to 1,25-(OH)<sub>2</sub>D<sub>3</sub>, these analogs are slightly less active in binding to the vitamin D receptor, in causing HL-60 differentiation, and are slightly less active in in vitro transcription assays using the 24-hydroxylase promoter attached to a luciferase reporter gene. Of considerable importance is that these analogs, given to rats at daily doses of up to 70  $\mu$ g/kg of body weight per day, are either unable or only slightly able to raise serum calcium concentration

but are nevertheless able to suppress parathyroid hormone levels in plasma up to 100% and induce 24-hydroxylase mRNA in skin. Because of their

ability to act in vivo without raising serum calcium levels, they may be of considerable interest for the systemic treatment of diseases such as psoriasis, cancer, and secondary hyperparathyroidism of renal failure, where a rise in serum calcium is undesirable.

- ST dihydroxyvitamin D3 analog calcium blood rat  
IT mRNA  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(24-hydroxylase; biol. active noncalcemic analogs of  
1 $\alpha$ ,25-dihydroxyvitamin D with an abbreviated side chain containing no  
hydroxyl as evaluated in rat, HL-60 and osteosarcoma 17/2.8 cells)
- IT Blood serum  
Bone  
Cell differentiation  
Human  
(biol. active noncalcemic analogs of 1 $\alpha$ ,25-dihydroxyvitamin D  
with an abbreviated side chain containing no hydroxyl as evaluated in rat,  
HL-60 and osteosarcoma 17/2.8 cells)
- IT Vitamin D receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(biol. active noncalcemic analogs of 1 $\alpha$ ,25-dihydroxyvitamin D  
with an abbreviated side chain containing no hydroxyl as evaluated in rat,  
HL-60 and osteosarcoma 17/2.8 cells)
- IT Skin  
(keratinocyte, 24-hydroxylase mRNA; biol. active noncalcemic analogs of  
1 $\alpha$ ,25-dihydroxyvitamin D with an abbreviated side chain containing no  
hydroxyl as evaluated in rat, HL-60 and osteosarcoma 17/2.8 cells)
- IT 3352-57-6, Hydroxyl, biological studies 7440-70-2, Calcium, biological  
studies 9002-64-6, Parathyroid hormone 32222-06-3,  
1 $\alpha$ ,25-Dihydroxyvitamin D3 67272-34-8, Calcitriol 24-hydroxylase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(biol. active noncalcemic analogs of 1 $\alpha$ ,25-dihydroxyvitamin D  
with an abbreviated side chain containing no hydroxyl as evaluated in rat,  
HL-60 and osteosarcoma 17/2.8 cells)
- IT 524067-20-7 524067-21-8 524067-22-9  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(biol. active noncalcemic analogs of 1 $\alpha$ ,25-dihydroxyvitamin D  
with an abbreviated side chain containing no hydroxyl as evaluated in rat,  
HL-60 and osteosarcoma 17/2.8 cells)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- IT 524067-20-7 524067-21-8 524067-22-9  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL



(Biological study)

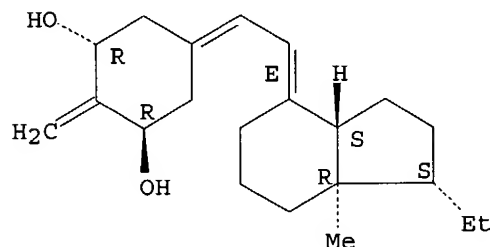
(biol. active noncalcemic analogs of  $1\alpha,25$ -dihydroxyvitamin D  
with an abbreviated side chain containing no hydroxyl as evaluated in rat,  
HL-60 and osteosarcoma 17/2.8 cells)

RN 524067-20-7 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

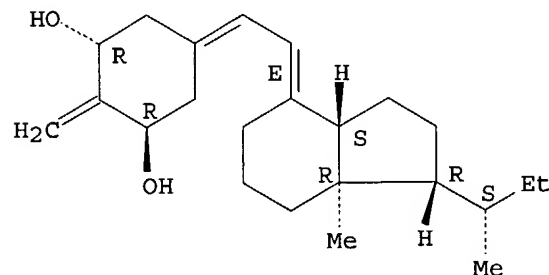


RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

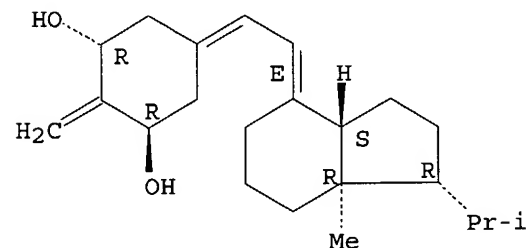


RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



AN 2004:191311 HCAPLUS  
DN 140:386155  
ED Entered STN: 10 Mar 2004  
TI Molecular structure of rat vitamin D receptor ligand binding domain  
complexed with 2-carbon-substituted vitamin D3 hormone analogs and a  
LXXLL-containing coactivator peptide  
AU Vanhooke, Janeen L.; Benning, Matthew M.; Bauer, Cary B.; Pike, J. Wesley;  
DeLuca, Hector F.  
CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706,  
USA  
SO Biochemistry (2004), 43(14), 4101-4110  
CODEN: BICHAW; ISSN: 0006-2960  
PB American Chemical Society  
DT Journal  
LA English  
CC 2-2 (Mammalian Hormones)  
AB The authors have determined the crystal structures of the ligand binding domain  
(LBD) of the rat vitamin D receptor in ternary complexes with a synthetic  
LXXLL-containing peptide and the following four ligands: 1 $\alpha$ ,25-  
dihydroxyvitamin D3; 2-methylene-19-nor-(20S)-1 $\alpha$ ,25-dihydroxyvitamin  
D3 (2MD); 1 $\alpha$ -hydroxy-2-methylene-19-nor-(20S)-  
bishomopregnacalciferol (2Mbisp), and 2 $\alpha$ -methyl-19-nor-1 $\alpha$ ,25-  
dihydroxyvitamin D3 (2AM20R). The conformation of the LBD is identical in  
each complex. Binding of the 2-carbon-modified analogs does not change  
the positions of the amino acids in the ligand binding site and has no  
effect on the interactions in the coactivator binding pocket. The CD ring  
of the superpotent analog, 2MD, is tilted within the binding site relative  
to the other ligands in this study and to (20S)-1 $\alpha$ ,25-  
dihydroxyvitamin D3. The aliphatic side chain of 2MD follows a different  
path within the binding site; nevertheless, the 25-hydroxyl group at the  
end of the chain occupies the same position as that of the natural ligand,  
and the hydrogen bonds with histidines 301 and 393 are maintained. 2Mbisp  
binds to the receptor despite the absence of the 25-hydroxyl group. A  
water mol. is observed between His 301 and His 393 in this structure, and it  
preserves the orientation of the histidines in the binding site. Although  
the  $\alpha$ -chair conformer is highly favored in solution for the A ring of  
2AM20R, the crystal structures demonstrate that this ring assumes the  
 $\beta$ -chair conformation in all cases, and the 1 $\alpha$ -hydroxyl group is  
equatorial. The peptide folds as a helix and is anchored through hydrogen  
bonds to a surface groove formed by helices 3, 4, and 12. Electrostatic  
and hydrophobic interactions between the peptide and the LBD stabilize the  
active receptor conformation. This stabilization appears necessary for  
crystal growth.  
ST vitamin D3 receptor protein motif peptide complex crystal structure  
IT Transcription factors  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(DRIP 205; mol. structure of rat vitamin D receptor ligand binding  
domain complexed with 2-carbon-substituted vitamin D3 hormone analogs  
and LXXLL-containing coactivator peptide)  
IT Bond length  
Hydrogen bond  
Hydroxyl group  
Protein motifs  
(mol. structure of rat vitamin D receptor ligand binding domain  
complexed with 2-carbon-substituted vitamin D3 hormone analogs and  
LXXLL-containing coactivator peptide)  
IT Vitamin D receptors  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(mol. structure of rat vitamin D receptor ligand binding domain  
complexed with 2-carbon-substituted vitamin D3 hormone analogs and  
LXXLL-containing coactivator peptide)

IT Helix (conformation)  
(protein; mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

IT Bond angle  
(torsional; mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

IT 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3 131875-08-6, KH1060  
134523-84-5, MC1288 213250-70-5 217446-51-0 **524067-21-8**  
685835-65-8  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

IT 71-00-1, L-Histidine, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(residues 301 and 393; mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 524067-21-8

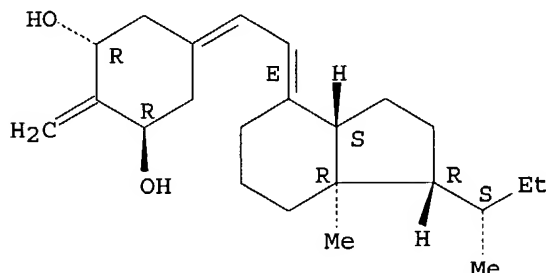
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)

(mol. structure of rat vitamin D receptor ligand binding domain  
 complexed with 2-carbon-substituted vitamin D3 hormone analogs and  
 LXXLL-containing coactivator peptide)

RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-  
 1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L8 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:855808 HCAPLUS

DN 139:345953

ED Entered STN: 31 Oct 2003

TI (20S)-1 $\alpha$ -Hydroxy-2 $\alpha$ -methyl--19-nor-vitamin D3 and  
 (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl--19-nor-vitamin D3, and  
 pharmaceutical uses

IN Deluca, Hector F.; Sicinski, Rafal R.; Grzywacz,  
 Pawel K.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-593

ICS A61P017-06; A61P019-10; A61P035-00; A61P037-06

CC 1-12 (Pharmacology)

Section cross-reference(s): 32, 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088977	A1	20031030	WO 2003-US8423	20030320 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
 UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

US 2003203882	A1	20031030	US 2002-127180	20020422 <--
US 2004152675	A1	20040805	US 2004-762618	20040122 <--
US 2004152676	A1	20040805	US 2004-762710	20040122 <--
US 2004152677	A1	20040805	US 2004-762906	20040122 <--
US 2004152678	A1	20040805	US 2004-762911	20040122 <--
US 2004152679	A1	20040805	US 2004-763023	20040122 <--
US 2004152680	A1	20040805	US 2004-763029	20040122 <--
PRAI US 2002-127180	A	20020422	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003088977	ICM	A61K031-593
	ICS	A61P017-06; A61P019-10; A61P035-00; A61P037-06
AB	The invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D3 and pharmaceutical uses therefor. These compds. exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases, e.g. psoriasis, as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compds. also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases, e.g. osteoporosis. Compound preparation is described.	
ST	norvitamin D3 deriv prepn therapeutic; antitumor skin condition therapy norvitamin D3 deriv; immune disease osteoporosis norvitamin D3 deriv; metabolic bone disease norvitamin D3 deriv	
IT	Animal cell line (HL-60; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Bone (bone mass increase; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Biological transport (calcium; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Intestine, neoplasm (colon; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Drugs (gastrointestinal; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Transplant and Transplantation (host-vs.-graft reaction; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Hydration, physiological (inadequate dermal hydration; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Cell differentiation (inducers; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Intestine, disease (inflammatory; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Sebum (insufficient secretion; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Osteoporosis (low bone turnover osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)	
IT	Anti-inflammatory agents Antiasthmatics Antidiabetic agents	

Antirheumatic agents  
 Antitumor agents  
 Asthma  
 Autoimmune disease  
 Cell differentiation  
 Diabetes mellitus  
 Human  
 Inflammation  
 Leukemia  
 Lupus erythematosus  
 Mammary gland, neoplasm  
 Monocyte  
 Multiple sclerosis  
 Osteomalacia  
 Prostate gland, neoplasm  
 Psoriasis  
 Rheumatoid arthritis  
 Transplant rejection  
 (nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Vitamin D receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Drug delivery systems  
 (oral; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Bone, disease  
 (osteopenia; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Drug delivery systems  
 (parenterals; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Osteoporosis  
 (postmenopausal; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Myelocyte  
 (promyelocyte; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Aging, animal  
 (senile osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Steroids, biological studies  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (steroid-induced osteoporosis; nor-vitamin D3 derivs. and  
 pharmaceutical uses)  
 IT Drug delivery systems  
 (topical; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Drug delivery systems  
 (transdermal; nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT Skin  
 (wrinkles and other conditions; nor-vitamin D3 derivs. and  
 pharmaceutical uses)  
 IT 7440-70-2, Calcium, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT 618104-20-4P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT 50-14-6, Vitamin D2 98-59-9, p-Toluenesulfonyl chloride 98-88-4,  
 Benzoyl chloride 4237-74-5 213250-64-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (nor-vitamin D3 derivs. and pharmaceutical uses)  
 IT 64190-52-9P 66774-70-7P 66774-71-8P 115527-12-3P 145354-28-5P  
 235108-01-7P 235108-02-8P 618104-21-5P 618104-22-6P  
 618879-43-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (nor-vitamin D3 derivs. and pharmaceutical uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

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IT 618104-22-6P

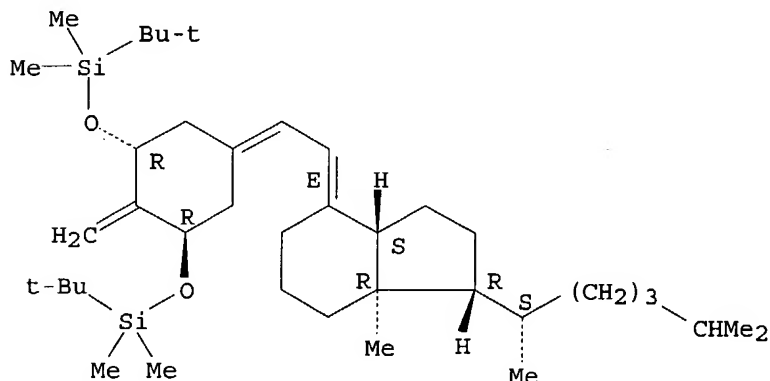
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 HCAPLUS

CN Silane, [[(1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-  
5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L8 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:796312 HCAPLUS  
DN 139:307926  
ED Entered STN: 10 Oct 2003  
TI Process for preparing 1 $\alpha$ -hydroxy-2-methylene-19-nor-  
homopregnacalciferol from vitamin D2  
IN Deluca, Hector F.; Gowlugari, Sumithra; Sicinski, Rafal  
R.  
PA Wisconsin Alumni Research Foundation, USA  
SO U.S. Pat. Appl. Publ., 9 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
IC ICM A61K031-59  
ICS C07C401-00  
NCL 514167000; 552653000  
CC 32-7 (Steroids)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003191095	A1	20031009	US 2003-397135	20030326 <--
	US 6774251	B2	20040810		
	WO 2003084925	A1	20031016	WO 2003-US9186	20030326 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,				

UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

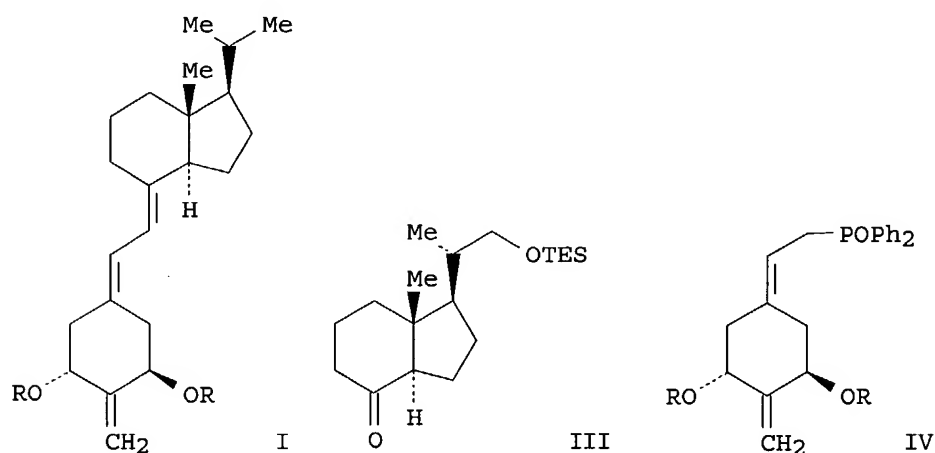
PRAI US 2002-369159P P 20020329 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003191095	ICM	A61K031-59
	ICS	C07C401-00
	NCL	514167000; 552653000

OS CASREACT 139:307926; MARPAT 139:307926

GI



- AB The present invention discloses a process for preparing 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol [I; R = H (II)]. The method includes the steps of ozonating vitamin D<sub>2</sub> to bicyclic ketone III, condensing III with an allylic phosphine oxide IV (R = TBDMS) to produce a protected 19-nor-pregnacalciferol analog, thereafter cleaving the protecting group to form 22-alc., converting the alc. to an ester, reducing the ester to 17 $\alpha$ -isopropyl-19-nor-vitamin D analog I [R = TBDMS (V)], and finally deprotecting V to form II.
- ST homopregnacalciferol hydroxy methylene nor prepn vitamin D<sub>2</sub>; norhomopregnacalciferol prepn norpregnacalciferol analog
- IT Hydrolysis  
 (acid; preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D<sub>2</sub>)
- IT Hydrolysis  
 (base; preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D<sub>2</sub>)
- IT Sulfonylation  
 (mesylation; preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D<sub>2</sub>)
- IT Ozonization  
 (preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D<sub>2</sub>)
- IT Condensation reaction  
 (stereoselective; between bicyclic ketone and an allylic phosphine oxide in preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol)
- IT Oxidation  
 Reduction



(stereoselective; in preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol)

IT Sulfonation

(tosylation; in preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D<sub>2</sub>)

IT 591-51-5, Phenyllithium

RL: RGT (Reagent); RACT (Reactant or reagent)

(for condensation between bicyclic ketone and an allylic phosphine oxide in preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol)

IT 64190-52-9P 610304-66-0P 610304-67-1P 610304-68-2P 610304-69-3P  
610304-70-6P **610304-71-7P**

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

IT 524067-22-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

IT	50-14-6, Vitamin D2	98-59-9, p-Toluene sulfonyl chloride	79271-56-0,
	Triethylsilyl trifluoromethanesulfonate	213250-64-7	

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol  
from vitamin D2)

IT 429-41-4, Tetrabutylammonium fluoride 16853-85-3, Lithium aluminum hydride 20039-37-6 24057-28-1, Pyridinium p-toluenesulfonate

RL: RGT (Reagent); RACT (Reactant or reagent)  
(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol  
from vitamin D2)

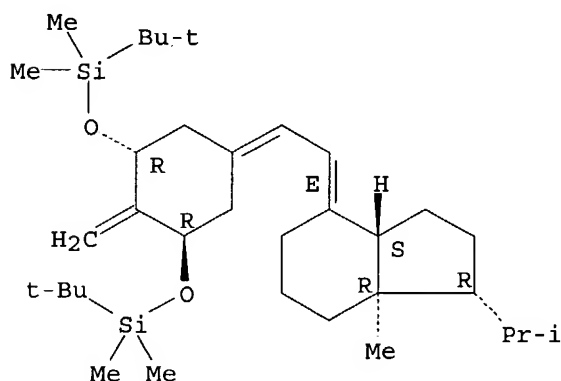
IT 610304-71-7P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 610304-71-7 HCAPLUS

CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



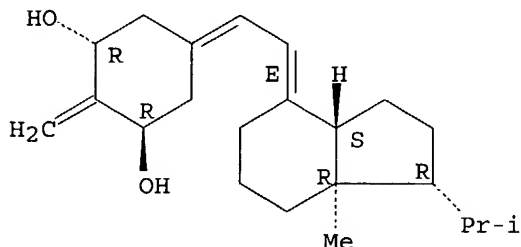
IT 524067-22-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

## (Preparation)

(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol  
from vitamin D2)

RN 524067-22-9 HCAPLUS

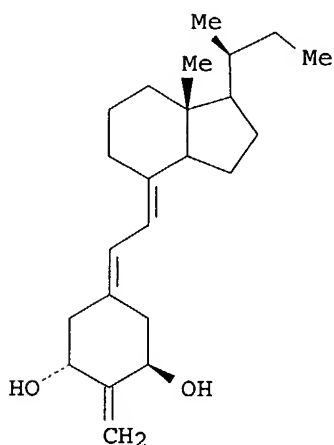
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA  
INDEX NAME)Absolute stereochemistry.  
Double bond geometry as shown.

L8 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2003:491175 HCAPLUS  
 DN 139:53211  
 ED Entered STN: 27 Jun 2003  
 TI (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its  
 therapeutic applications in the treatment of cancer, skin diseases and  
 immune disorders  
 IN Deluca, Hector F.; Plum, Lori A.; Clagett-Dame, Margaret;  
 Thoden, James B.; Holden, Hazel M.; Gowlugari, Sumithra; Grzywacz,  
 Pawel  
 PA Wisconsin Alumni Research Foundation, USA  
 SO PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07C401-00  
 ICS A61K031-59; A61P011-06; A61P017-06; A61P035-00; A61P029-00;  
 A61P037-00  
 CC 32-7 (Steroids)  
 Section cross-reference(s): 1, 2, 63, 75  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003051828	A2	20030626	WO 2002-US39715	20021212 <--
	WO 2003051828	A3	20030912		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2003158157	A1	20030821	US 2002-78204	20020218 <--
	US 6627622	B2	20030930		
	US 2003204103	A1	20031030	US 2002-317467	20021212 <--
	US 2004033998	A1	20040219	US 2003-462272	20030616 <--
PRAI	US 2001-341138P	P	20011213	<--	

US 2002-78204 A 20020218 <--  
 CLASS  
 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES  
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 WO 2003051828 ICM C07C401-00  
 ICS A61K031-59; A61P011-06; A61P017-06; A61P035-00;  
 A61P029-00; A61P037-00

GI

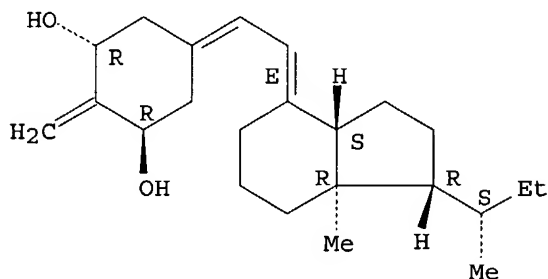


- AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2-methylene-19-norbishomopregnacalciferol (I), pharmaceutical uses therefor, and a method of purifying this compound to obtain it in crystalline form. I exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. I also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.
- ST homopregnacalciferol cancer immune disease skin calcemia treatment; crystal structure homopregnacalciferol purifn renal osteodystrophy treatment
- IT Anti-inflammatory agents  
 Antiasthmatics  
 Antidiabetic agents  
 Antirheumatic agents  
 Antitumor agents  
 Human  
 Monocyte  
 Psoriasis  
 ((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Vitamin D receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Skin, disease  
 (aging, wrinkles; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Intestine, neoplasm

- (colon, treatment; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Skin  
(firmness; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Transplant and Transplantation  
(host-vs.-graft reaction, treatment; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Intestine, disease  
(inflammatory, treatment; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Sebum  
(insufficient secretion; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Crystal structure  
Crystallization  
(of (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems  
(oral; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems  
(parenterals; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Bone, disease  
(renal osteodystrophy, treatment; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems  
(topical; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems  
(transdermal; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Asthma  
Autoimmune disease  
Diabetes mellitus  
Leukemia  
Mammary gland, neoplasm  
Multiple sclerosis  
Prostate gland, neoplasm  
Rheumatoid arthritis  
Transplant rejection  
(treatment; (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT 524067-21-8, (20S)-1 $\alpha$ -Hydroxy-2-methylene-19-norbishomopregnacalciferol  
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

- IT 60-29-7, Diethylether, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 75-09-2, Dichloromethane, uses 141-78-6, Ethyl acetate, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (for purifying (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol)
- IT 7440-70-2, Calcium, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (transport; effects of (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol on calcium levels in relation to their potential therapeutic uses)
- IT 524067-21-8, (20S)-1 $\alpha$ -Hydroxy-2-methylene-19-norbishomopregnacalciferol  
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- RN 524067-21-8 HCAPLUS
- CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L8 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2003:390842 HCAPLUS  
 DN 138:363223  
 ED Entered STN: 22 May 2003  
 TI Methods for the uses of 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in the treatment of cancer, skin diseases and immune disorders  
 IN Deluca, Hector F.; Plum, Lori A.; Clagett-Dame, Margaret  
 PA Wisconsin Alumni Research Foundation, USA  
 SO U.S., 13 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-59  
 ICS C07C401-00  
 NCL 514167000; 552653000  
 CC 2-10 (Mammalian Hormones)  
 Section cross-reference(s): 14  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6566352	B1	20030520	US 2002-77916	20020218 <--
	WO 2003075932	A1	20030918	WO 2002-US39390	20021210 <--
	WO 2003075932	C1	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-77916 A 20020218 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6566352	ICM	A61K031-59
	ICS	C07C401-00
	NCL	514167000; 552653000

AB This invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-pregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

ST vitamin D deriv treatment cancer immune diseases skin calcemia

IT Skin, disease  
 (aging, wrinkles; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Vitamin D receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (binding of vitamin D compds.; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Bone  
 (calcium mobilization; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Intestine  
 (calcium transport; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Intestine, neoplasm  
 (colon; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Skin, disease  
 (dry; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Cell differentiation  
 (effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Transplant and Transplantation  
 (graft-vs.-host reaction; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Intestine, disease  
 (inflammatory; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Sebum  
(insufficient secretion; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Anti-inflammatory agents  
Antiasthmatics  
Antidiabetic agents  
Antirheumatic agents  
Antitumor agents  
Asthma  
Autoimmune disease  
Diabetes mellitus  
Human  
Inflammation  
Leukemia  
Lupus erythematosus  
Mammary gland, neoplasm  
Multiple sclerosis  
Prostate gland, neoplasm  
Psoriasis  
Rheumatoid arthritis  
Skin, disease  
Skin preparations (pharmaceutical)  
Transplant rejection  
(methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Bone, disease  
(renal osteodystrophy; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Skin, disease  
(slackness; methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT 1406-16-2D, Vitamin D, derivs. 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3 130447-37-9 524067-21-8 524067-22-9  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT 524067-20-7  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(transport; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE  
(1) Anon; WO 9601811 1996 HCAPLUS  
(2) Brown; Kidney International 1990, V38(Suppl 29), PS-22  
(3) Deluca; US 4800198 A 1989 HCAPLUS  
(4) Deluca; US 5089641 A 1992 HCAPLUS  
(5) Deluca; US 5536713 A 1996 HCAPLUS  
(6) Deluca; US 5578587 A 1996 HCAPLUS  
(7) Deluca; US 5587497 A 1996 HCAPLUS  
(8) Deluca; US 5843928 A 1998 HCAPLUS  
(9) Deluca; US 5936133 A 1999 HCAPLUS  
(10) Deluca; US 5945410 A 1999 HCAPLUS  
(11) Hareau; Tetrahedron Letters 2000, V41, P2385 HCAPLUS  
(12) Hennessy; US 5840718 A 1998 HCAPLUS  
(13) Kutner; US 5817648 A 1998 HCAPLUS

(14) Miyamoto; US 4666634 A 1987 HCAPLUS

(15) Posner; J Org Chem 1995, V60(4617), P4617

(16) Sicinski; J Med Chem 1998, V41, P4662 HCAPLUS

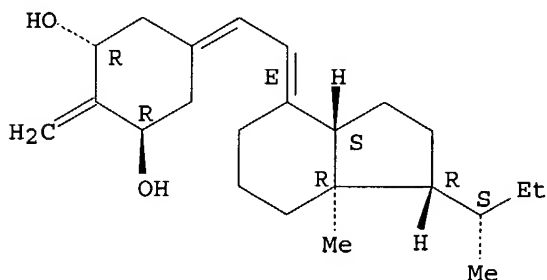
IT 524067-21-8 524067-22-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(effects of vitamin D compds. on cell differentiation and calcium  
levels in relation to their potential pharmaceutical uses)

RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
(CA INDEX NAME)

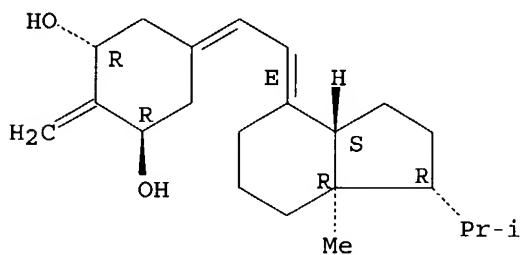
Absolute stereochemistry.  
Double bond geometry as shown.



RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 524067-20-7

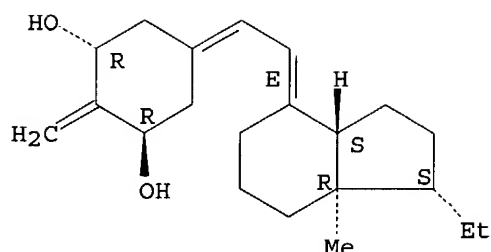
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol  
in treatment of cancer, skin diseases and immune disorders)

RN 524067-20-7 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.





L8 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2003:249861 HCAPLUS  
 DN 139:317525  
 ED Entered STN: 01 Apr 2003  
 TI Interaction between vitamin D receptor and vitamin D ligands  
 two-dimensional alanine scanning mutational analysis  
 AU Choi, Mihwa; Yamamoto, Keiko; Itoh, Toshimasa; Makishima, Makoto;  
 Mangelsdorf, David J.; Moras, Dino; DeLuca, Hector F.; Yamada,  
 Sachiko  
 CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental  
 University, Chiyoda-ku, Tokyo, 101-0062, Japan  
 SO Chemistry & Biology (2003), 10(3), 261-270  
 CODEN: CBOLE2; ISSN: 1074-5521  
 PB Cell Press  
 DT Journal  
 LA English  
 CC 2-1 (Mammalian Hormones)  
 AB We present a new method to investigate the details of interaction between  
 vitamin D nuclear receptor (VDR) and various ligands, namely a  
 two-dimensional alanine scanning mutational anal. In this method, the  
 transactivation of various ligands is studied in conjunction with a series  
 of alanine scanning mutations of the residues lining the ligand binding  
 pocket (LBP) of VDR, and the complete set of results is profiled in a  
 patch table. We investigated examples from four structurally diverse  
 groups of known VDR ligands: the native vitamin D hormone and two compds.  
 with the same side chain configuration; four 20-epi compds.; three 19-nor  
 compds.; and two nonsecosteroids. The patch table of the results  
 indicates characteristics of each group in terms of its interaction with  
 18 LBP residues. We demonstrate the validity of this approach by  
 application to docking studies of the two nonsecosteroids.  
 ST vitamin D receptor structure activity ligand binding alanine mutagenesis  
 IT Simulation and Modeling, physicochemical  
 (docking models of VDR ligands; two-dimensional alanine scanning  
 mutational anal. and modeling of the interaction between vitamin D  
 receptor (VDR) its ligands)  
 IT Structure-activity relationship  
 (ligand-binding; two-dimensional alanine scanning mutational anal. and  
 modeling of the interaction between vitamin D receptor (VDR) its  
 ligands)  
 IT Protein motifs  
 (of VDR; two-dimensional alanine scanning mutational anal. and modeling  
 of the interaction between vitamin D receptor (VDR) its ligands)  
 IT Mutagenesis  
 (site-directed; two-dimensional alanine scanning mutational anal. and  
 modeling of the interaction between vitamin D receptor (VDR) its  
 ligands)  
 IT Configuration  
 Secondary structure  
 (two-dimensional alanine scanning mutational anal. and modeling of the  
 interaction between vitamin D receptor (VDR) its ligands)

IT Vitamin D receptors  
RL: PRP (Properties)  
(two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

IT 56-41-7, L-Alanine, properties  
RL: PRP (Properties)  
(mutational anal.; two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

IT 434-13-9 1553-56-6 32222-06-3 103909-75-7 104121-92-8  
131875-08-6, KH 1060 134523-84-5 177766-94-8 195051-26-4  
213250-70-5 213312-43-7 **524067-22-9**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (30) Yamamoto, K; J Med Chem 1996, V39, P2727 HCAPLUS
- (31) Yamamoto, K; J Org Chem 1993, V58, P2530 HCAPLUS
- (32) Yamamoto, K; Proc Natl Acad Sci USA 2000, V97, P1467 HCAPLUS

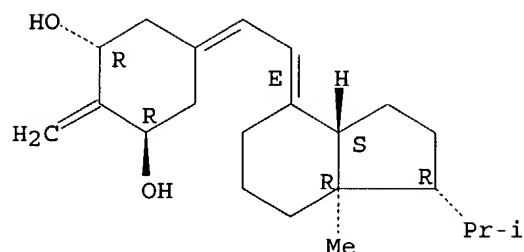
IT **524067-22-9**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L8 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:332679 HCAPLUS  
DN 136:335278  
ED Entered STN: 03 May 2002  
TI 1 $\alpha$ -Hydroxy-2-methylene-19-nor-homopregnacalciferol and its  
therapeutic uses  
IN DeLuca, Hector F.; Sicinski, Rafal R.; Gowlugari,  
Sumithra; Plum, Lori A.; Clagett-Dame, Margaret  
PA USA  
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 657,828.  
CODEN: USXXCO  
DT Patent  
LA English  
IC ICM A61K031-59  
NCL 514167000  
CC 1-12 (Pharmacology)  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 2002052350	A1	20020502	US 2001-878438	20010611 <--
	US 6440953	B2	20020827		
	US 2002183289	A1	20021205	US 2002-165123	20020607 <--
	US 6579861	B2	20030617		
PRAI	US 2000-657828	A2	20000908	<--	
	US 2001-878438	A3	20010611	<--	

CLASS			
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
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US 2002052350	ICM	A61K031-59	
	NCL	514167000	
US 2002052350	ECLA	A61K007/48C4D	
US 2002183289	ECLA	A61K007/48C4D	

AB	The invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and its pharmaceutical uses. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.
ST	hydroxymethylenenorhomopregnacalciferol cell proliferation differentiation therapeutic; cancer skin disease immune disorder hydroxymethylenenorhomopregnacalciferol; renal osteodystrophy hydroxymethylenenorhomopregnacalciferol
IT	Animal cell line (HL-60; hydroxymethylenenorhomopregnacalciferol and therapeutic use)
IT	Animal cell line (LLC; hydroxymethylenenorhomopregnacalciferol and therapeutic use)
IT	Animal cell line

(ROS; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Skin, disease  
(aging, wrinkles; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Bone  
(calcium mobilization; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Biological transport  
(calcium; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Intestine, neoplasm  
(colon, inhibitors; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents  
(colon; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drugs  
(gastrointestinal; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Transplant and Transplantation  
(host-vs.-graft reaction; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Anti-inflammatory agents  
 Antiasthmatics  
 Antidiabetic agents  
 Antirheumatic agents  
 Autoimmune disease  
 Human  
 Lupus erythematosus  
 Psoriasis  
 Skin  
 Transcription, genetic  
 Transplant rejection  
 (hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Vitamin D receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Cell differentiation  
(inducers; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Intestine, disease  
(inflammatory; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents  
(leukemia; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents  
(mammary gland; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Mammary gland  
 Prostate gland  
 (neoplasm, inhibitors; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems  
(oral; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems  
(parenterals; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents  
(prostate gland; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Bone, disease  
(renal osteodystrophy; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Sebum  
(secretion; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Multiple sclerosis  
(therapeutic agents; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems  
(topical; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems  
(transdermal; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3 213250-70-5  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT 403647-27-8  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

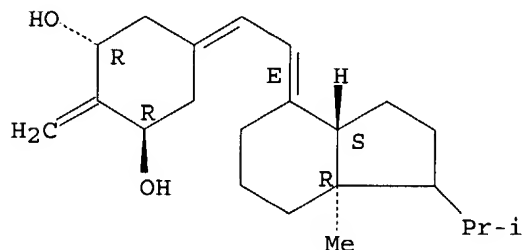
IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(intestinal transport; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT 403647-27-8  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 403647-27-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L8 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:184908 HCAPLUS

DN 136:226818

ED Entered STN: 15 Mar 2002

TI 1 $\alpha$ -Hydroxy-2-methylene-19-nor-homopregnacalciferol and its therapeutic applications

IN Deluca, Hector F.; Sicinski, Rafal R.; Gowlugari, Sumithra; Plum, Lori A.; Clagett-Dame, Margaret

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 31 pp.  
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-59  
ICS C07C401-00

CC 1-12 (Pharmacology)  
Section cross-reference(s): 2, 62, 63

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

PI WO 2002020021 A1 20020314 WO 2001-US18710 20010611 <--  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,  
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
AU 2001075445 A5 20020322 AU 2001-75445 20010611 <--  
EP 1315504 A1 20030604 EP 2001-942154 20010611 <--  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
BR 2001013703 A 20030722 BR 2001-13703 20010611 <--  
JP 2004512276 T2 20040422 JP 2002-524505 20010611 <--  
PRAI US 2000-657828 A 20000908 <--  
WO 2001-US18710 W 20010611 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002020021	ICM	A61K031-59
	ICS	C07C401-00
JP 2004512276	FTERM	4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/DA15; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA02; 4C086/ZA59; 4C086/ZA66; 4C086/ZA89; 4C086/ZA96; 4C086/ZB08; 4C086/ZB15; 4C086/ZB26; 4C086/ZB27; 4C086/ZC23; 4C086/ZC35; 4H006/AA01; 4H006/AA03; 4H006/AB22; 4H006/AB27; 4H006/AB28; 4H006/UA13
AB	This invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte this evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.	
ST	homopregnacalciferol deriv therapeutic cancer immune disorder; renal osteodystrophy treatment homopregnacalciferol deriv; skin disease treatment homopregnacalciferol deriv	
IT	Anti-inflammatory agents Antiasthmatics Antidiabetic agents Antirheumatic agents Antitumor agents Human Monocyte (1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Vitamin D receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Animal cell line (HL-60, cell differentiation; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Transcriptional regulation (activation; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Bone (calcium mobilization; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	

IT Kidney  
(cells; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Intestine, neoplasm  
(colon, inhibitors; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents  
(colon; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Skin  
(conditions wrinkles and slack skin, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Immunity  
(disorder, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Skin, disease  
(dry, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Transplant and Transplantation  
(host-vs.-graft reaction, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Cell differentiation  
(inducers; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Intestine, disease  
(inflammatory, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Cell proliferation  
(inhibition, of undifferentiated cells; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Sebum  
(insufficient secretion of, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents  
(leukemia; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents  
(mammary gland; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Mammary gland  
Prostate gland  
(neoplasm, inhibitors; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antidiabetic agents  
Drug delivery systems  
(oral; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Drug delivery systems  
(parenterals; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents  
(prostate gland; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Bone, disease  
(renal osteodystrophy, treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Drug delivery systems  
(topical; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Drug delivery systems  
(transdermal; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Autoimmune disease

Lupus erythematosus  
 Multiple sclerosis  
 Psoriasis  
 Skin, disease  
 Transplant rejection  
 (treatment of; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol  
 and therapeutic applications)

IT 403647-27-8

RL: BSU (Biological study, unclassified); COS (Cosmetic use); DMA (Drug  
 mechanism of action); PAC (Pharmacological activity); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and  
 therapeutic applications)

IT 7440-70-2, Calcium, biological studies

RL: ADV (Adverse effect, including toxicity); BSU (Biological study,  
 unclassified); BIOL (Biological study)  
 (calcemic; 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and  
 therapeutic applications)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Brown, A; KIDNEY INTERNATIONAL 1990, V38(29), PS-22
- (2) Hareau, G; TETRAHEDRON LETTERS 2000, V41(14), P2385 HCAPLUS
- (3) Rafal, S; US 5843928 A 1998 HCAPLUS
- (4) Rafal, S; US 5945410 A 1999 HCAPLUS
- (5) Sicinski; JOURNAL OF MEDICINAL CHEMISTRY 1998, V41, P4662 HCAPLUS
- (6) Sicinski, R; US 5936133 A 1999 HCAPLUS

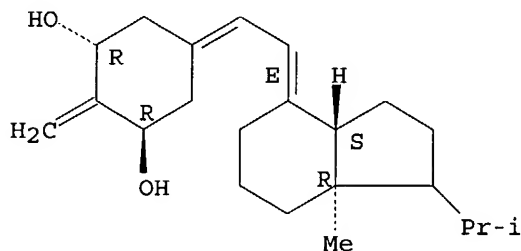
IT 403647-27-8

RL: BSU (Biological study, unclassified); COS (Cosmetic use); DMA (Drug  
 mechanism of action); PAC (Pharmacological activity); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and  
 therapeutic applications)

RN 403647-27-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-  
 (1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



=> fil uspatall

FILE 'USPATFULL' ENTERED AT 10:23:11 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:23:11 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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L10 ANSWER 1 OF 18 USPATFULL on STN



AN 2004:197374 USPATFULL  
 TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses  
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Sicinski, Rafal R., Warsaw, POLAND  
 Grzywacz, Pawel K., Madison, WI, UNITED STATES  
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)  
 PI US 2004152680 A1 20040805  
 AI US 2004-763029 A1 20040122 (10)  
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 981

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

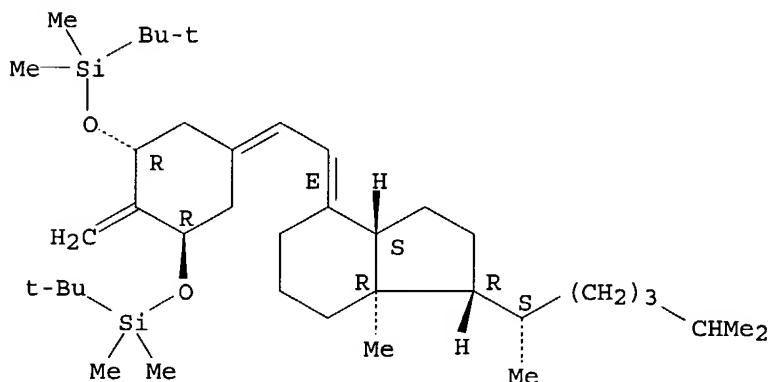
IT 618104-22-6P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L10 ANSWER 2 OF 18 USPATFULL on STN

AN 2004:197373 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Sicinski, Rafal R., Warsaw, POLAND  
 Grzywacz, Pawel K., Madison, WI, UNITED STATES  
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)  
 PI US 2004152679 A1 20040805  
 AI US 2004-763023 A1 20040122 (10)  
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

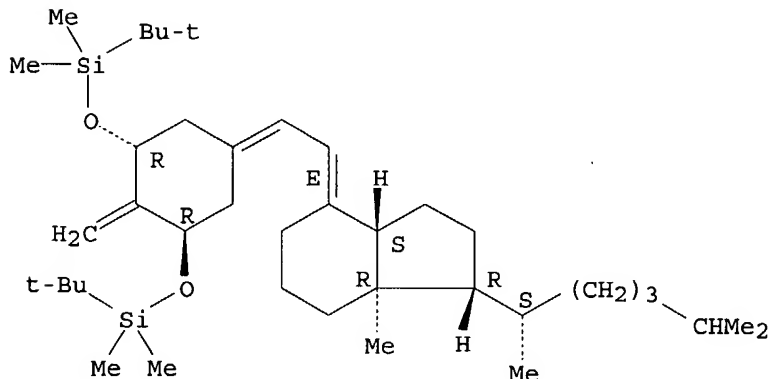
IT 618104-22-6P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[[1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L10 ANSWER 3 OF 18 USPATFULL on STN

AN 2004:197372 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Sicinski, Rafal R., Warsaw, POLAND  
 Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)  
 PI US 2004152678 A1 20040805  
 AI US 2004-762911 A1 20040122 (10)  
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

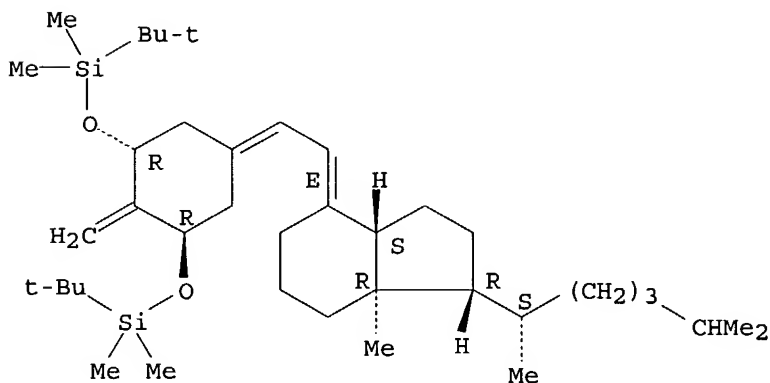
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[[1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 4 OF 18 USPATFULL on STN

AN 2004:197371 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152677 A1 20040805

AI US 2004-762906 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 77  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Page(s)  
 LN.CNT 980

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

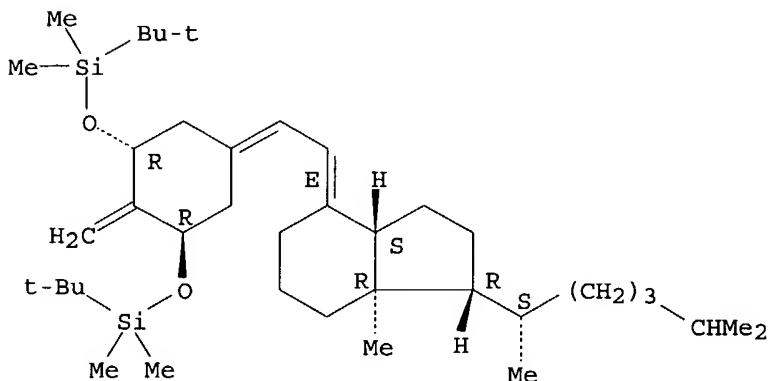
IT 618104-22-6P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[[1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L10 ANSWER 5 OF 18 USPATFULL on STN

AN 2004:197370 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152676 A1 20040805

AI US 2004-762710 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 978

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

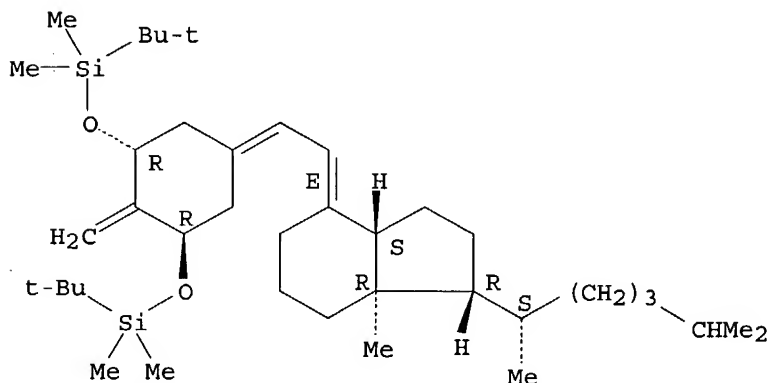
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[[1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 6 OF 18 USPATFULL on STN

AN 2004:197369 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3  
and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S.  
corporation)

PI US 2004152675 A1 20040805

AI US 2004-762618 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

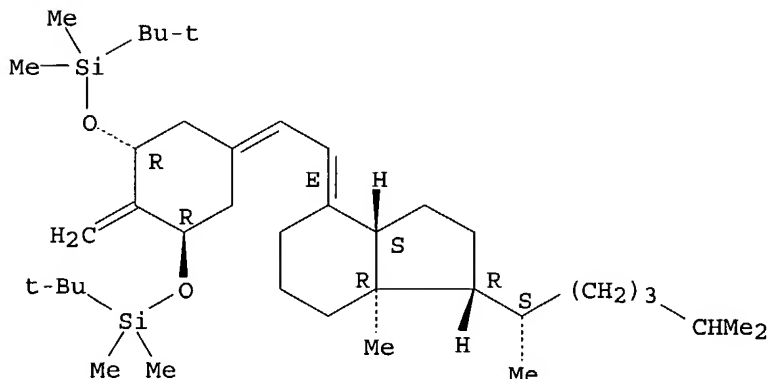
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 7 OF 18 USPATFULL on STN

AN 2004:45005 USPATFULL

TI (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)

PI US 2004033998 A1 20040219

AI US 2003-462272 A1 20030616 (10)

RLI Division of Ser. No. US 2002-78204, filed on 18 Feb 2002, GRANTED, Pat. No. US 6627622

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 33

ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)

LN.CNT 500

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

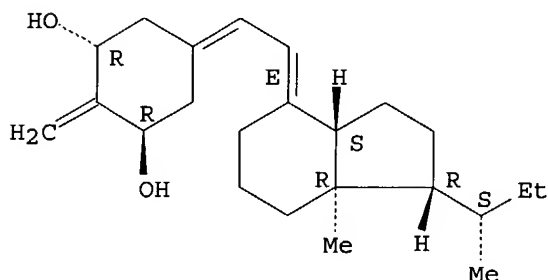
IT 524067-21-8, (20S)-1 $\alpha$ -Hydroxy-2-methylene-19-norbishomopregnacalciferol

((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

RN 524067-21-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 8 OF 18 USPATFULL on STN

AN 2003:289341 USPATFULL

TI 2-Methylene-19-nor-20(S)-1 $\alpha$ -hydroxy-bis-homo-pregnacalciferol in crystalline form

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
Thoden, James B., Madison, WI, UNITED STATES  
Holden, Hazel M., Fitchburg, WI, UNITED STATES  
Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES  
Gowlugari, Sumithra, Madison, WI, UNITED STATES  
Grzywacz, Pawel, Madison, WI, UNITED STATES

PI US 2003204103 A1 20031030

AI US 2002-317467 A1 20021212 (10)

PRAI US 2001-341138P 20011213 (60)

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 2169

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of purifying 2-methylene-19-nor-20(S)-1 $\alpha$ -hydroxy-bis-homo-pregnacaciferol to obtain 2-methylene-19-nor-20(S)-1 $\alpha$ -hydroxy-bis-homo-pregnacalciferol in crystalline form. The method includes the steps of boiling a solvent such as acetone under inert atmosphere, dissolving a product containing 2-methylene-19-nor-20(S)-1 $\alpha$ -hydroxy-bis-homo-pregnacalciferol to be purified in the solvent, cooling the solvent and dissolved product below ambient temperature for a sufficient amount of time to form a precipitate of 2-methylene-19-nor-20(S)-1 $\alpha$ -hydroxy-bis-homo-pregnacalciferol crystals, and recovering the 2-methylene-19-nor-20(S)-1 $\alpha$ -hydroxy-bis-homo-pregnacalciferol crystals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

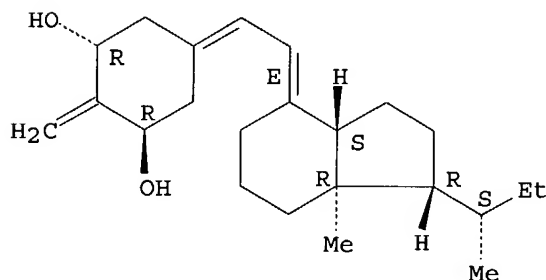
IT 524067-21-8, (20S)-1 $\alpha$ -Hydroxy-2-methylene-19-norbishomopregnacalciferol

((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

RN 524067-21-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-(9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 9 OF 18 USPATFULL on STN

AN 2003:289123 USPATFULL

TI (20S) 1 $\alpha$ -hydroxy-2 $\alpha$ -methyl and 2 $\beta$ -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PI US 2003203882 A1 20031030

AI US 2002-127180 A1 20020422 (10)

DT Utility

FS APPLICATION

LREP KINNEY & LANGE, P.A., THE KINNEY & LANGE BUILDING, 312 SOUTH THIRD STREET, MINNEAPOLIS, MN, 55415-1002

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2 $\alpha$ -methyl-19-nor-vitamin D.sub.3 and (20S)-1 $\alpha$ -hydroxy-2 $\beta$ -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing



use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

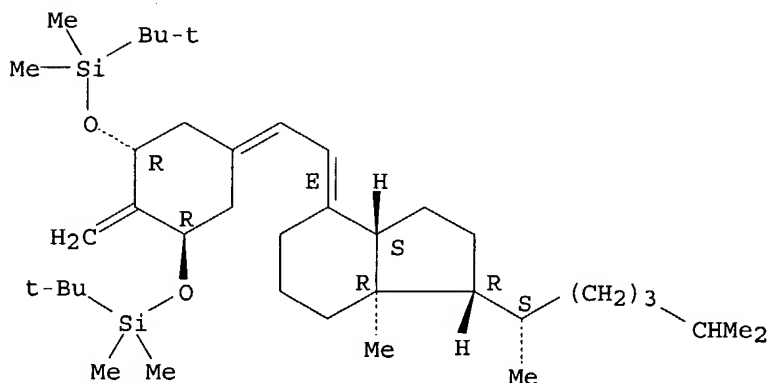
IT 618104-22-6P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 $\alpha$ ,3 $\beta$ ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 10 OF 18 USPATFULL on STN

AN 2003:271487 USPATFULL

TI Method of synthesizing 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Gowlugari, Sumithra, Fremont, CA, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

PI US 2003191095 A1 20031009

US 6774251 B2 20040810

AI US 2003-397135 A1 20030326 (10)

PRAI US 2002-369159P 20020329 (60)

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 423

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of making 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol. The method includes the steps of condensing a bicyclic ketone with an allylic phosphine oxide to produce a protected 19-nor-pregnacalciferol analog, thereafter cleaving the protecting group to form 22-alcohol, converting the alcohol to an ester, reducing the ester to 17 $\beta$ -isopropyl-19-nor-vitamin D analog, and finally deprotecting the 17 $\beta$ -isopropyl derivative to form the desired compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

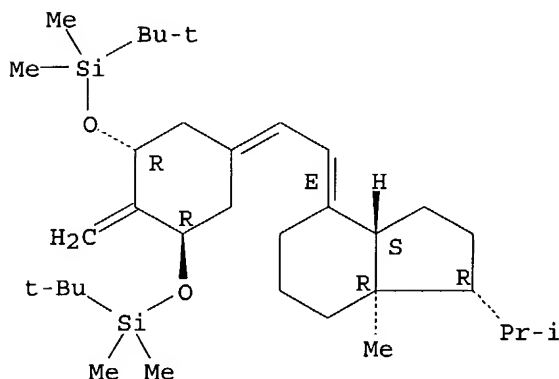
IT 610304-71-7P

(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 610304-71-7 USPTAFULL

CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



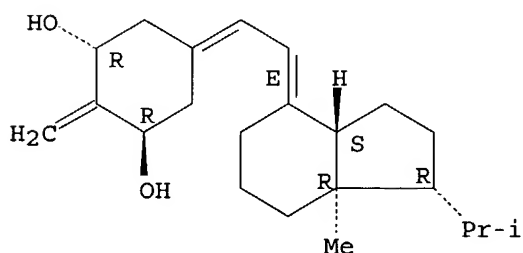
IT 524067-22-9P

(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 524067-22-9 USPTAFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 11 OF 18 USPTAFULL on STN

AN 2003:226344 USPTAFULL

TI (20S)-1ALPHA-HYDROXY-2-METHYLENE-19-NOR-BISHOMOPREGNACALCIFEROL AND ITS USES

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Madison, WI, UNITED STATES

PI US 2003158157 A1 20030821

US 6627622 B2 20030930

AI US 2002-78204 A1 20020218 (10)

DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 33  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Page(s)  
 LN.CNT 500

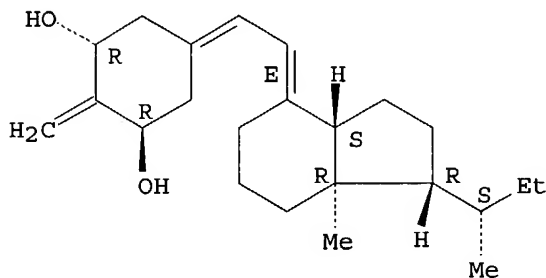
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 524067-21-8, (20S)-1 $\alpha$ -Hydroxy-2-methylene-19-norbishomopregnacalciferol  
 ((20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)  
 RN 524067-21-8 USPATFULL  
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L10 ANSWER 12 OF 18 USPATFULL on STN  
 AN 2003:137075 USPATFULL  
 TI 1  $\alpha$ -hydroxy-2-methylene-19-nor-pregnacalciferol and its uses  
 IN DeLuca, Hector F., Deerfield, WI, United States  
 Plum, Lori A., Madison, WI, United States  
 Clagett-Dame, Margaret, Madison, WI, United States  
 PA Wisconsin Alumni Research Foudation, Madison, WI, United States (U.S. corporation)  
 PI US 6566352 B1 20030520  
 AI US 2002-77916 20020218 (10)  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Qazi, Sabiha  
 LREP Andrus, Sceales, Starke & Sawall, LLP  
 CLMN Number of Claims: 33  
 ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 494

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-pregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

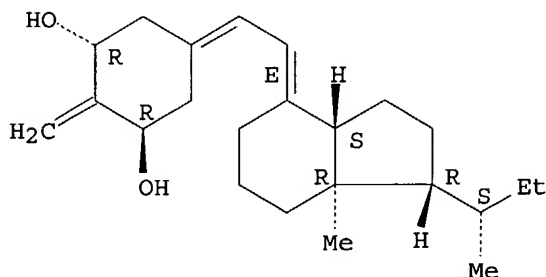
IT 524067-21-8 524067-22-9

(effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

RN 524067-21-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
(CA INDEX NAME)

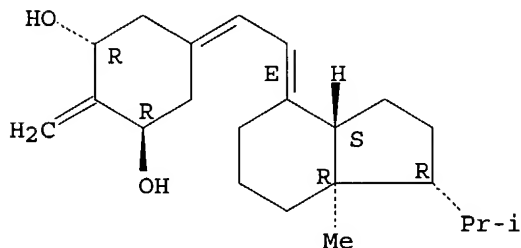
Absolute stereochemistry.  
Double bond geometry as shown.



RN 524067-22-9 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 524067-20-7

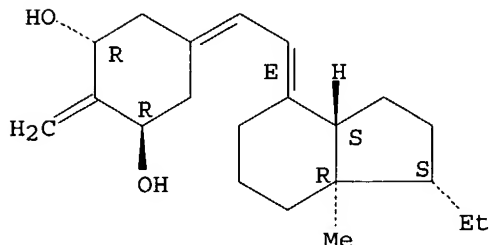
(methods for using 1 $\alpha$ -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

RN 524067-20-7 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 13 OF 18 USPATFULL on STN  
 AN 2002:323123 USPATFULL  
 TI 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses  
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Sicinski, Rafal R., Warsaw, POLAND  
 Gowlugari, Sumithra, Madison, WI, UNITED STATES  
 Plum, Lori A., Madison, WI, UNITED STATES  
 Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES  
 PA Wisconsin Alumni Research Foundation of Madison (U.S. corporation)  
 PI US 2002183289 A1 20021205  
 US 6579861 B2 20030617  
 AI US 2002-165123 A1 20020607 (10)  
 RLI Division of Ser. No. US 2001-878438, filed on 11 Jun 2001, GRANTED, Pat.  
 No. US 6440953 Continuation-in-part of Ser. No. US 2000-657828, filed on  
 8 Sep 2000, ABANDONED  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 33  
 ECL Exemplary Claim: 1  
 DRWN 7 Drawing Page(s)  
 LN.CNT 503

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

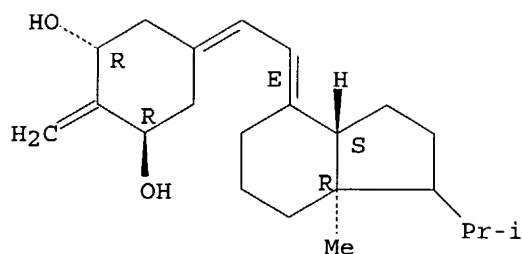
IT 403647-27-8

(1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and  
therapeutic applications)

RN 403647-27-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 14 OF 18 USPATFULL on STN

AN 2002:99449 USPATFULL

TI 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES

PI US 2002052350 A1 20020502

US 6440953 B2 20020827

AI US 2001-878438 A1 20010611 (9)

RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000,  
PENDING

DT Utility

FS APPLICATION

LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 East  
Wisconsin Avenue, Suite 1100, Milwaukee, WI, 53202-4178

CLMN Number of Claims: 33

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 502

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 403647-27-8

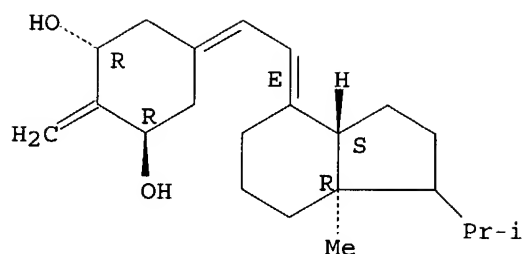
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 403647-27-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 15 OF 18 USPAT2 on STN  
 AN 2003:271487 USPAT2  
 TI Method of synthesizing 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol  
 IN DeLuca, Hector F., Deerfield, WI, United States  
 Gowlugari, Sumithra, Fremont, WI, United States  
 Sicinski, Rafal R., Warsaw, POLAND  
 PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)  
 PI US 6774251 B2 20040810  
 AI US 2003-397135 20030326 (10)  
 PRAI US 2002-369159P 20020329 (60)  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Qazi, Sabiha  
 LREP Andrus, Sceales, Starke & Sawall, LLP  
 CLMN Number of Claims: 15  
 ECL Exemplary Claim: 1  
 DRWN 0 Drawing Figure(s); 0 Drawing Page(s)  
 LN.CNT 433  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB A method of making 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol. The method includes the steps of condensing a bicyclic ketone with an allylic phosphine oxide to produce a protected 19-nor-pregnacalciferol analog, thereafter cleaving the protecting group to form 22-alcohol, converting the alcohol to an ester, reducing the ester to 17 $\beta$ -isopropyl-19-nor-vitamin D analog, and finally deprotecting the 17 $\beta$ -isopropyl derivative to form the desired compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

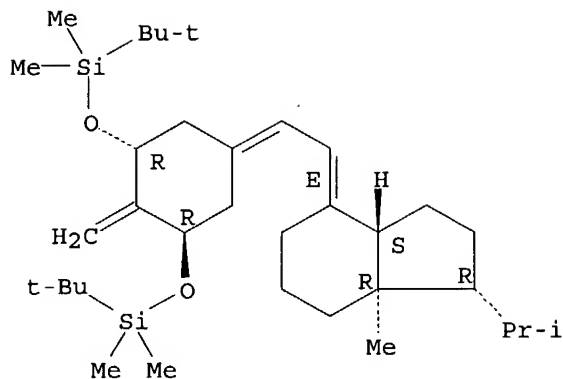
IT 610304-71-7P

(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 610304-71-7 USPAT2

CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



IT 524067-22-9P

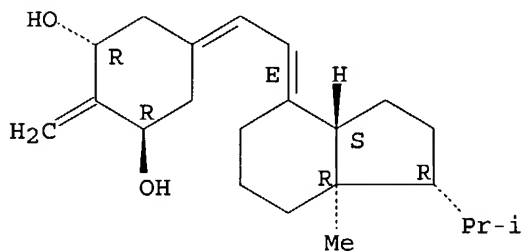
(preparation of 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 524067-22-9 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 16 OF 18 USPAT2 on STN

AN 2003:226344 USPAT2

TI (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Madison, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6627622 B2 20030930

AI US 2002-78204 20020218 (10)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Padmanabhan, Sreeni; Assistant Examiner: Hui, San-ming

LREP Andrus, Sceales, Starke &amp; Sawall, LLP

CLMN Number of Claims: 1

ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 419

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of



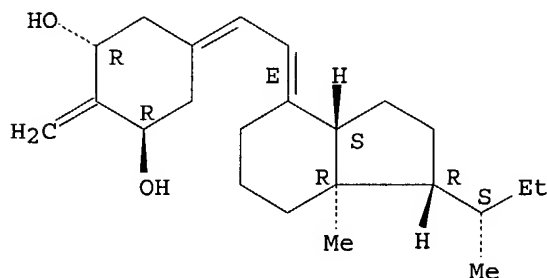
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(20S)-1 $\alpha$ -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

RN 524067-21-8 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L10 ANSWER 17 OF 18 USPAT2 on STN

AN 2002:323123 USPAT2

TI 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Deerfield, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6579861 B2 20030617

AI US 2002-165123 20020607 (10)

RLI Division of Ser. No. US 2001-878438, filed on 11 Jun 2001, now patented,  
Pat. No. US 6440953 Continuation-in-part of Ser. No. US 2000-657828,  
filed on 8 Sep 2000, now abandoned

DT      Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 7 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 432

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the

monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 403647-27-8

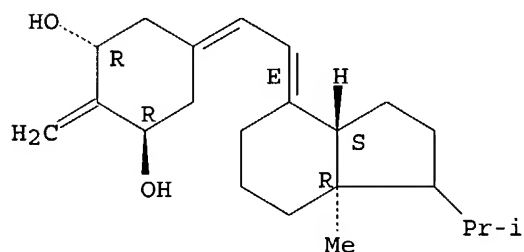
(1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

RN 403647-27-8 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 18 OF 18 USPAT2 on STN

AN 2002:99449 USPAT2

TI 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Deerfield, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6440953 B2 20020827

AI US 2001-878438 20010611 (9)

RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 26

ECL Exemplary Claim: 1

DRWN 7 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 485

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 403647-27-8

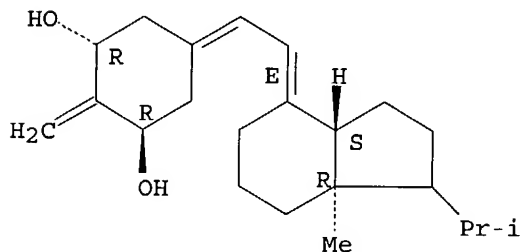
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 403647-27-8 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



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FILE 'REGISTRY' ENTERED AT 13:53:01 ON 25 AUG 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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DICTIONARY FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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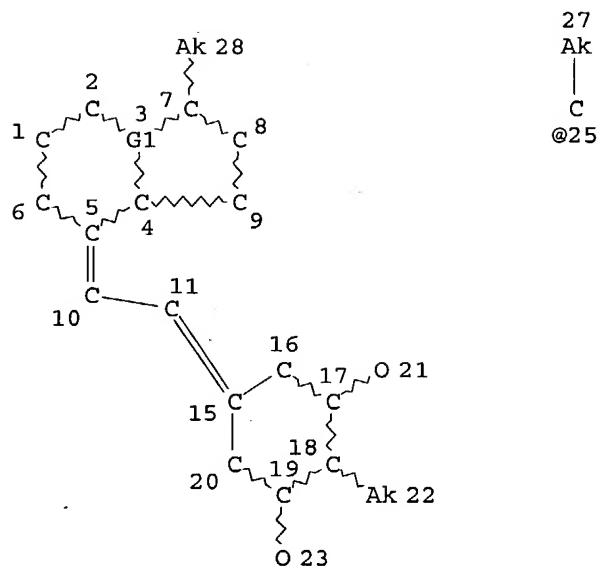
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L1 STR



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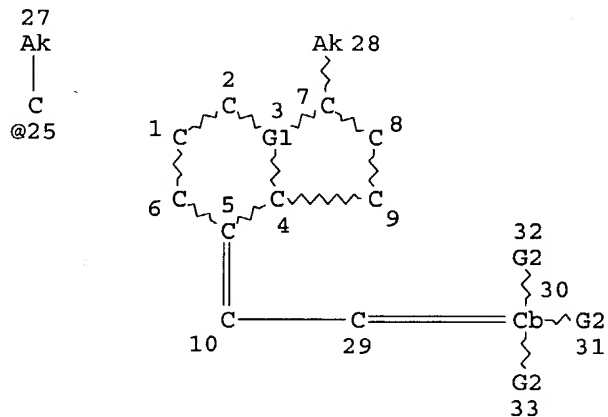
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L3      STR

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GRAPH ATTRIBUTES:
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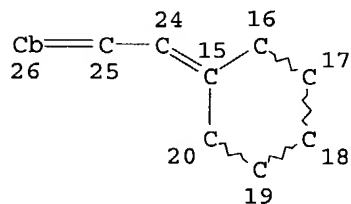
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L9 STR



NODE ATTRIBUTES:

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GGCAT IS PCY AT 26

DEFAULT ECLEVEL IS LIMITED

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RSPEC 19

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

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0 ANSWERS

SEARCH TIME: 00.00.01

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